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		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L9	(sliwkowski)adj(mark)adj(x)	19
<input type="checkbox"/>	L8	(brunetta)adj(paul)adj(g)	6
<input type="checkbox"/>	L7	L6 and ErbB2	1
<input type="checkbox"/>	L6	L5 and antibody	54
<input type="checkbox"/>	L5	(non-malignant)adj(disease)same(treatment)	119
<input type="checkbox"/>	L4	L3 and anti-ErbB2	12
<input type="checkbox"/>	L3	(ErbB2)same(psoriasis)	108
<input type="checkbox"/>	L2	(treatment)same(psoriasis)same(ErbB2)adj(antibod?)	1
		<i>DB=USPT; PLUR=YES; OP=OR</i>	
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=> s Erbb2 antibod?
L1 247 ERBB2 ANTIBOD?

=> s l1 and treatment
L2 96 L1 AND TREATMENT

=> s l2 and non-malignant
L3 1 L2 AND NON-MALIGNANT

=> d l3 cbib abs

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
2004:467984 Document No. 141:22217 Therapy of **non-malignant** diseases or disorders with anti-**ErbB2** **antibodies**. Sliwkowski, Mark X.; Brunetta, Paul G. (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized antibodies to HER2. In one example, an anti-HER2 antibody is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes **treatment** of **non-malignant** indications, such as psoriasis, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with anti-**ErbB2** **antibodies** (e.g. rhuMAb 2C4).

=> s antibod?
L4 2735552 ANTIBOD?

=> s l4 and anti-HER2
L5 1117 L4 AND ANTI-HER2

=> s l5 and anti-p185neu
L6 0 L5 AND ANTI-P185NEU

=> s l5 and anti-p185
L7 8 L5 AND ANTI-P185

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8 4 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> d l8 1-4 cbib abs

L8 ANSWER 1 OF 4 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

2001:973008 The Genuine Article (R) Number: 499TJ. Weekly paclitaxel as first-line chemotherapy and trastuzumab in patients with advanced breast cancer - A Hellenic Cooperative Oncology Group phase II study. Fountzilas G (Reprint); Tsavdaridis D; Kalogera-Fountzila A; Christodoulou C; Timotheadou E; Kalofonos C; Kosmidis P; Adamou A; Papakostas P; Gogas H; Stathopoulos G; Razis E; Bafaloukos D; Skarlos D. Aristotelian Univ Thessaloniki, AHEPA Hosp, Oncol Sect, Dept Internal Med 1, GR-54006 Thessaloniki, Macedonia, Greece (Reprint); Aristotelian Univ Thessaloniki, Sch Med, GR-54006 Thessaloniki, Greece; IKA Hosp, Thessaloniki, Greece; Medicalenter Athens, Athens, Greece; Univ Patras, Sch Med, RIO Hosp, GR-26110 Patras, Greece; HYGEIA Med Ctr, Athens, Greece; Bank Cyprus Oncol Ctr, Nicosia, Cyprus; Ippokrat Hosp, Athens, Greece; Laiko Hosp, Athens, Greece; Metaxa Canc Hosp, Piraeus, Greece. ANNALS OF ONCOLOGY (2001) Vol. 12, No. 11, pp. 1545-1551. ISSN: 0923-7534. Publisher: KLUWER ACADEMIC PUBL, VAN GODEWIJCKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Aim: to evaluate the activity and acute toxicity of the combination of weekly paclitaxel as first-line chemotherapy and trastuzumab, in patients with HER-2/neu overexpressing advanced breast cancer (ABC).

Background: Weekly paclitaxel has been shown to be a well tolerated treatment with considerable activity in patients with ABC. Clinical trials with transtuzumab, a humanized anti-p185

HER-2/neu monoclonal antibody have demonstrated that this agent produces objective responses in patients with ABC.

Patients and methods: From December 1998 to April 2000, 34 patients with HER-2/neu overexpressing ABC were treated with weekly paclitaxel; given by one-hour infusion at a dose of 90 mg/m² immediately followed by trastuzumab, 4 mg/kg as a loading dose and 2 mg/kg i.v. given over 30 min, thereafter weekly for at least 12 weeks. Expression of HER-2/neu was determined by immunohistochemical analysis on fixed, paraffin-embedded tissues. Eligible patients were required to have greater than or equal to 25% stained tumor cells.

Results: Thirty-three patients completed at least 12 weeks of combined treatment. After completion of the 12th week of treatment, four patients (12%) achieved complete and 17 (50%) partial response. Median duration of response was 11.6 months. More frequent side effects included anemia (56%), neutropenia (27%), peripheral neuropathy (78%), diarrhea (30%), alopecia (70%), arthralgias/myalgias (62%), fatigue (59%) and hypersensitivity reactions (62%). Median time to progression was nine months while median survival had not been reached

Conclusions: The combination of weekly paclitaxel and trastuzumab is a safe and active regimen for patients with HER-2/neu overexpressing ABC. Randomized phase III studies with this combination are warranted.

L8 ANSWER 2 OF 4 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 1

2000062571 EMBASE Rationally designed anti-HER2/neu peptide mimetic disables p185(HER2/neu) tyrosine kinases in vitro and in vivo. Park B.-W.; Zhang H.-T.; Wu C.; Berezov A.; Zhang X.; Dua R.; Wang Q.; Kao G.; O'Rourke D.M.; Greene M.I.; Murali R.. M.I. Greene, Dept. of Pathology and Lab. Medicine, Ctr. for Receptor Biol./Cell Growth, Univ. of Pennsylvania School of Med., 36th and Hamilton Walk, Philadelphia, PA 19104, United States. greene@reo.med.upenn.edu. Nature Biotechnology Vol. 18, No. 2, pp. 194-198 2000.

Refs: 43.

ISSN: 1087-0156. CODEN: NABIF

Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20000224

AB Monoclonal antibodies specific for the p185(HER2/neu) growth factor receptor represent a significant advance in receptor-based therapy for p185(HER2/neu)-expressing human cancers. We have used a structure-based approach to develop a small (1.5 kDa) exocyclic

anti-HER2/neu peptide mimic (AHNP) functionally similar to an **anti-p185(HER2/neu)** monoclonal **antibody**, 4D5 (Herceptin). The AHNP mimetic specifically binds to p185(HER2/neu) with high affinity ($K(D) = 300 \text{ nM}$). This results in inhibition of proliferation of p185(HER2/neu)-overexpressing tumor cells, and inhibition of colony formation in vitro and growth of p185(HER2/neu)-expressing tumors in athymic mice. In addition, the mimetic sensitizes the tumor cells to apoptosis when used in conjunction with ionizing radiation or chemotherapeutic agents. A comparison of the molar quantities of the Herceptin **antibody** and the AHNP mimetic required for inhibiting cell growth and anchorage-independent growth showed generally similar activities. The structure-based derivation of the AHNP represents a novel strategy for the design of receptor-specific tumor therapies.

L8 ANSWER 3 OF 4 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 2

1999410901 EMBASE Dose escalation and pharmacokinetic study of a humanized **anti-HER2** monoclonal **antibody** in patients with HER2/neu-overexpressing metastatic breast cancer. Tokuda Y.; Watanabe T.; Omuro Y.; Ando M.; Katsumata N.; Okumura A.; Ohta M.; Fujii H.; Sasaki Y.; Niwa T.; Tajima T.. Y. Tokuda, Department of Surgery, Tokai University School of Medicine, Bohseidai Isehara, Kanagawa 259-1193, Japan. British Journal of Cancer Vol. 81, No. 8, pp. 1419-1425 1999.

Refs: 24.

ISSN: 0007-0920. CODEN: BJCAAI

Pub. Country: United Kingdom. Language: English. Summary Language: English.

ED Entered STN: 19991210

AB We conducted a phase I pharmacokinetic dose escalation study of a recombinant humanized **anti-p185(HER2)** monoclonal **antibody** (MKC-454) in 18 patients with metastatic breast cancer refractory to chemotherapy. Three or six patients at each dose level received 1, 2, 4 and 8 mg kg⁻¹ of MKC-454 as 90-min intravenous infusions. The first dose was followed in 3 weeks by nine weekly doses. Target trough serum concentration has been set at 10 µg ml⁻¹ based on in vitro observations. The mean value of minimum trough serum concentrations at each dose level were 3.58 ± 0.63, 6.53 ± 5.26, 40.2 ± 7.12 and 87.9 ± 23.5 µg ml⁻¹ respectively. At 2 mg kg⁻¹, although minimum trough serum concentrations were lower than the target trough concentration with a wide range of variation, trough concentrations increased and exceeded the target concentration, as administrations were repeated weekly. Finally 2 mg kg⁻¹ was considered to be sufficient to achieve the target trough concentration by the weekly dosing regimen. One patient receiving 1 mg kg⁻¹ had grade 3 fever, one at the 1 mg kg⁻¹ level had severe fatigue defined as grade 3, and one at 8 mg kg⁻¹ had severe bone pain of grade 3. No **antibodies** against MKC-454 were detected in any patients. Objective tumour responses were observed in two patients one receiving 4 mg kg⁻¹ had a partial response in lung metastases and the other receiving 8 mg kg⁻¹ had a complete response in soft tissue metastases. These results indicate that MKC-454 is well tolerated and effective in patients with refractory metastatic breast cancers overexpressing the HER2 proto-oncogene. Further evaluation of this agent with 2-4 mg kg⁻¹ weekly intravenous infusion is warranted.

L8 ANSWER 4 OF 4 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 3

1999241383 EMBASE Neutralization of complement regulatory proteins augments lysis of breast carcinoma cells targeted with rhumAb **anti-HER2**. Jurianz K.; Maslak S.; Garcia-Schuler H.; Fishelson Z.; Kirschfink M.. M. Kirschfink, Institute of Immunology, University of Heidelberg, Im Neuenheimer Feld 305, Heidelberg 69120, Germany. k92@ix.urz.uni-heidelberg.de. Immunopharmacology Vol. 42, No. 1-3, pp. 209-218 1999.

Refs: 31.

ISSN: 0162-3109. CODEN: IMMUDP

S 0162-3109(99)00006-5. Pub. Country: Netherlands. Language: English.
Summary Language: English.

ED Entered STN: 19990802

AB The capacity of recombinant human monoclonal **anti-p185**
(HER2) IgG (rhumAb **anti-HER2**) to activate human
complement was investigated. Complement activation by rhumAb **anti**
-HER2 on various human breast carcinoma cell lines resulted in
deposition of complement proteins on these cells. Complement activation
was also observed in a solid-phase binding assay, in which purified
p185(HER2) was immobilized onto a microtiter plate. rhumAb **anti**-
HER2 induced some complement-mediated tumor cell lysis by rabbit
complement, but not by human complement. Analysis of membrane complement
regulatory proteins (mCRP) on breast carcinoma cells revealed a
heterogenous expression of CD46, CD55 and CD59. After blocking the mCRP
activity with specific **antibodies**, rhumAb **anti**-
HER2 induced about 15% lysis of p185(HER2)-expressing tumor cells.
Tumor cell sensitization with rabbit polyclonal anti-tumor antiserum
following mCRP neutralization, augmented cell lysis from 10 to 80%.
Expression of mCRP was upregulated by treatment with PMA, and correlated
with increased protection of the tumor cells from complement lysis. These
results suggest that humanized **antibodies** like rhumAb
anti-HER2 promote complement activation leading to tumor
cell phagocytosis and cell-mediated cytotoxicity. They further
demonstrate that a successful tumor immunotherapeutical approach, based on
antibody and complement treatment, requires mCRP neutralization.

=> s herceptin

L9 4927 HERCEPTIN

=> s l9 and treatment

L10 2284 L9 AND TREATMENT

=> s l10 and non-malignant

L11 1 L10 AND NON-MALIGNANT

=> d l11 cbib abs

L11 ANSWER 1 OF 1 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights
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2004421378 EMBASE Mammaglobin-based strategies for **treatment** of
breast cancer. Goedegebuure P.S.; Watson M.A.; Viehl G.T.; Fleming T.P..
P.S. Goedegebuure, Washington Univ. School of Medicine, Department of
Surgery, Alvin J. Siteman Cancer Center, St. Louis, MO 63110, United
States. goodegep@wustl.edu. Current Cancer Drug Targets Vol. 4, No. 6,
pp. 531-542 2004.
Refs: 71.

ISSN: 1568-0096. CODEN: CCDTB

Pub. Country: Netherlands. Language: English. Summary Language: English.

ED Entered STN: 20041021

AB Mammaglobin is a gene that is expressed almost exclusively in the normal
breast epithelium and human breast cancer. It is a member of the
secretoglobulin gene family and forms a heterodimer with lipophilin B. We
have focused on the tissue-specificity of mammaglobin as a potential
mechanism for the specific killing of breast cancer cells. By elucidating
the promoter region of mammaglobin, we hope to utilize this site as a
method for turning on the apoptosis inducer gene, Bax, in breast cancer
cells. The Bax gene will only be expressed at levels necessary to induce
apoptosis in mammaglobin positive cells. This would include >80% of all
breast cancer cells and some normal breast epithelium. This type of
targeted killing could be conceptualized as a biochemical astectomy; that
is, genetic ablation of breast tumor cells and perhaps **non**-
malignant breast epithelium while preserving the adipose and
stromal components of the breast. Work is also being done to address the
binding specificity of the secreted mammaglobin protein. There is early

evidence that the mammaglobin heterodimer may in fact bind to breast and breast cancer cells. If this finding is validated, this creates the possibility that mammaglobin can be tagged with a radioisotope or a toxin, so that binding of the tagged-mammaglobin complex results in the specific killing of that breast cancer cell. Finally, mammaglobin is being explored as a target for immune-based interventions. In vitro studies have demonstrated that T cell-mediated immune responses can be induced against mammaglobin-derived peptides expressed by MHC molecules on tumor cells and antigen-presenting cells. In summary, mammaglobin displays several unique features that make it a promising target for intervention.

=> s l10 and psoriasis

L12 30 L10 AND PSORIASIS

=> dup remove l12

PROCESSING COMPLETED FOR L12

L13 30 DUP REMOVE L12 (0 DUPLICATES REMOVED)

=> d l13 1-30 cbib abs

L13 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2005:216897 Document No. 142:298249 Use of siRNA for inhibiting GPC15 gene expression in **treatment** of cancer and other hyperproliferative disorders. O'Hagan, Ronan C.; Kannan, Karuppiyah; Bailey, David (Genpáth Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2005021724 A2 20050310, 55 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US27968 20040827. PRIORITY: US 2003-2003/PV498393 20030827.

AB The present invention provides use of siRNA for inhibiting GPC15 gene expression in **treatment** of cancer and other hyperproliferative disorders and methods for diagnosis. Nonhuman mammals harboring a genetic modification relating to the GP115 gene, and their use as exptl. cancer models, are disclosed.

L13 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2005:14184 Document No. 142:120497 Combination liposomal formulations comprising phospholipids. Jamil, Haris; Ahmad, Imran; Ahmad, Zafeer; Anyarambhatla, Gopal (Neopharm, Inc., USA). PCT Int. Appl. WO 2005000266 A2 20050106, 39 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US16413 20040522. PRIORITY: US 2003-2003/PV47266U 20030522; US 2003-2003/PV495260 20030813.

AB The present invention provides a composition comprising a physiol. acceptable carrier and two or more agents encapsulated in a liposome, wherein the combination of the two or more agents possess the following properties: (1) cytotoxicity to tumor cells, (2) nutritional properties, (3) use in application to nails, hair, skin or lips, or (4) activity against parasites and insects. The invention also provides a method of making such a composition. The invention further provides a method of treating cancer when the combination of the two or more agents is cytotoxic to tumor cells. For example, an initial formulation of liposome-encapsulated

paclitaxel (LEP) was prepared containing phosphatidylcholine, cholesterol and cardiolipin. Sucrose and tocopherol were added to the formulation as stabilizers in order to form a sterilized lyophilized cake. Either doxorubicin (0.5 to 1.5 mg/mL) or mitoxantrone (0.5 to 1.5 mg/mL) was dissolved in water, and the solution was employed to reconstitute the lyophilized LEP cakes. The drug to lipid ratio varied from 1:120 to 1:24 (weight/weight) for doxorubicin and 1:120 to 1:24 (weight/weight) for mitoxantrone.

The reconstitution of the LEP cake with doxorubicin or mitoxantrone solution resulted in entrapment of either of the additive drugs (doxorubicin or mitoxantrone) into the liposomal formulation of paclitaxel (LEP). Moreover, 78 to 100% of the additive drug was entrapped into the LEP at a drug to lipid ratio of 1:120 to 1:15 for mitoxantrone and 1:120 to 1:24 for doxorubicin. Presence of an addnl. drug, doxorubicin or mitoxantrone, did not alter entrapment efficiency of paclitaxel in liposomes, size or stability of liposomes. Paclitaxel content remained intact after entrapping mitoxantrone or doxorubicin. This suggested that both drugs can coexist in a single delivery system without compromising size, entrapment efficiency or stability of the liposomal formulation.

L13 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2005:1005963 Document No. 143:279399 antiangiogenic compounds for treating disorders associated with vascular permeability. Soker, Shay; Satchi-Fainaro, Ronit (USA). U.S. Pat. Appl. Publ. US 2005203013 A1 20050915, 43 pp., Cont.-in-part of Appl. No. PCT/US03/11265. (English). CODEN: USXXCO. APPLICATION: US 2004-962723 20041012. PRIORITY: US 2002-2002/PV37184W 20020411; WO 2003-US11265 20030411.

AB The invention relates to methods for decreasing or inhibiting disorders associated with vascular hyperpermeability and to methods of screening for compds. that affect permeability, angiogenesis and stabilize tight junctions. In one aspect of the invention there is provided a method of decreasing or inhibiting vascular hyperpermeability in an individual in need of such **treatment**. The method includes administering to the individual an effective amount of an antiangiogenic compound selected from the group consisting of endostatin, thrombospondin, angiostatin, tumstatin, arrestin, recombinant EPO and polymer conjugated TNP-470. Other antiangiogenic compds. are disclosed herein.

L13 ANSWER 4 OF 30 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

2005396799 EMBASE [Technologies of recombinant human antibodies]. LES TECHNOLOGIES DES ANTICORPS RECOMBINANTS HUMAINS. Mondon P.; Dubreuil O.; Bouayadi K.; Kharrat H.. P. Mondon, MilleGen, Prologue Biotech, rue Pierre et Marie Curie, 31682 Labège Cedex, France. philippe.mondon@millegen.com. Biofutur No. 258, pp. 34-40 2005.

Refs: 9.

ISSN: 0294-3506. CODEN: BIOFEM

Pub. Country: France. Language: French.

ED Entered STN: 20051006

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L13 ANSWER 5 OF 30 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

2005139063 EMBASE Overview of biologic agents in medicine and dermatology. Sobell J.M.. Dr. J.M. Sobell, SkinCare Physicians of Chestnut Hill, 1244 Boylston Street, Chestnut Hill, MA 02467, United States. jsobell@skincarephysicians.net. Seminars in Cutaneous Medicine and Surgery Vol. 24, No. 1, pp. 2-9 2005.

Refs: 45.

ISSN: 1085-5629. CODEN: SCMSFR

Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20050421

AB Three agents have recently been approved by the Food and Drug Administration for the **treatment** of chronic plaque **psoriasis**: alefacept, efalizumab, and etanercept. The field of

dermatology has now entered a new era, joining other disciplines of medicine that have been using biologic agents for decades. These new therapies offer psoriatic patients the potential for safe and effective long-term management of this disease. This article reviews how an increased understanding of the pathophysiology of **psoriasis** led to the development of these products. .COPYRGT. 2005 Elsevier Inc. All rights reserved.

L13 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:965067 Document No. 141:406039 Combinations for the **treatment** of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A. (Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.). PCT Int. Appl. WO 2004096224 A2 20041111, 101 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-EP4363 20040424. PRIORITY: EP 2003-9587 20030429; EP 2004-508 20040113; EP 2004-1171 20040121.

AB The present invention relates to a pharmaceutical combination for the **treatment** of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the **treatment** of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-**treatment** with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepn's. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

L13 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:802862 Document No. 141:290028 Short interfering RNA (siRNA) containing locked nucleosides for **treatment** of cancer and SARS. Elmen, Joacim; Wahlestedt, Claes; Liang, Zicai; Sorensen, Anders Malling; Orum, Henrik; Koch, Troels (Santaris Pharma A/S, Den.). PCT Int. Appl. WO 2004083430 A2 20040930, 82 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-DK192 20040322. PRIORITY: DK 2003-442 20030321; US 2003-2003/PV45688D 20030321; DK 2003-1625 20031031; DK 2004-145 20040130.

AB The present invention is directed to novel double-stranded short interfering (siRNA) analogs comprising locked nucleic acid (LNA) monomers. Such compds. induces sequence-specific post-transcriptional gene silencing in many organisms by a process known as RNA interference (RNAi). The compds. disclosed herein has improved properties compared to non-modified siRNAs and may, accordingly, be useful as therapeutic agents, e.g., in the **treatment** of cancers and severe acute respiratory syndrome (SARS). Thus, in vitro expts. showed that (1) 3'-end capping of siRNA antisense strands with ≥ 1 LNAs improves nuclease stability; (2) placing ≥ 1 LNAs at the 5'-end of the sense strand improves the potency of the siRNA; and (3) placing a thymidine or 5-methylcytidine LNA at positions 10 and/or 12 from the 5'-end in the sense strand reduces

off-target effects. A highly preferred siRNA would therefore contain at least one LNA at the 5'-end and 3'-end of the sense strand and at least one LNA at the 3'-end of the antisense strand.

L13 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:681663 Document No. 141:201271 Antisense oligonucleotides for modulation of survivin gene expression and **treatment** of cancers. Hansen, Bo; Thruue, Charlotte Albaek; Petersen, Kamille Dumong; Westergaard, Majken; Wissenbach, Margit (Santaris Pharma A/S, Den.). PCT Int. Appl. WO 2004069991 A2 20040819, 122 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-DK96 20040210. PRIORITY: DK 2003-183 20030210; DK 2003-1708 20031118.

AB Oligonucleotides directed against the survivin gene are provided for modulating the expression of survivin. The compns. comprise oligonucleotides, particularly antisense oligonucleotides, targeted to nucleic acids encoding the survivin. Methods of using these compds. for modulation of survivin expression and for the **treatment** of diseases associated with either overexpression of survivin, expression of mutated survivin, or both, are provided. Examples of diseases are cancer such as lung, breast, colon, prostate, pancreas, lung, liver, thyroid, kidney, brain, testes, stomach, intestine, bowel, spinal cord, sinuses, bladder, urinary tract or ovaries cancers. The oligonucleotides may be composed of deoxyribonucleosides, or a nucleic acid analog (e.g., locked nucleic acid), or a combination thereof. Thus, 16-nucleotide antisense oligonucleotide gapmers containing phosphorothioate linkages throughout, β -D-oxy-LNA wings, and DNA cores were prepared. These oligonucleotides, targeting various positions in the human TRX mRNA, inhibited TRX gene expression by 17 to 96% in prostate cancer cell lines.

L13 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:606538 Document No. 141:156105 Mutated human antibodies having variant Fc region with altered affinity to Fc γ RIIIA and Fc γ RIIA for treating cancer, infection and autoimmune disease. Stavenhagen, Jeffrey; Vijh, Sujata (Macrogenics, Inc., USA). PCT Int. Appl. WO 2004063351 A2 20040729, 267 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US643 20040109. PRIORITY: US 2003-2003/PV43949U 20030109; US 2003-2003/PV45604U 20030319; US 2003-2003/PV514549 20031023.

AB The present invention relates to mols., particularly polypeptides, more particularly Igs (e.g., antibodies), comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, which variant Fc region binds Fc γ RIIIA and/or Fc γ RIIA with a greater affinity, relative to a comparable mol. comprising the wild-type Fc region. The mols. of the invention are particularly useful in preventing, treating, or ameliorating one or more symptoms associated with a disease, disorder, or infection. The mols. of the invention are particularly useful for the **treatment** or prevention of a disease or disorder where an enhanced efficacy of effector cell function (e.g., ADCC) mediated by Fc γ R is desired, e.g., cancer, infectious disease, and in enhancing the therapeutic efficacy of therapeutic antibodies the effect of which is mediated by ADCC.

L13 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:493842 Document No. 141:48598 Human calcitonin receptor activity modifying protein genes GPC99 and GPC99a involved in hyperproliferative conditions, and methods and compns. for treating and diagnosing cancer. O'Hagan, Ronan C.; Kannan, Karuppiiah; Wang, Rijian (Genpath Pharmaceuticals, Incorporated, USA). PCT Int. Appl. WO 2004050834 A2 20040617, 80 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL; PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37813 20031126. PRIORITY: US 2002-2002/PV429877 20021127.

AB This invention provides methods and compns. for treating hyperproliferative conditions such as cancer using reagents relating to the GPC99 or GPC99a gene, which encodes calcitonin receptor activity modifying protein 2 or 3 (RAMP2 or RAMP3) resp. GPC99 and GPC99a are identified by MaSS (Mammalian Second Site Suppression) screening and are mapped to human chromosome 17q12-q21.1 and 7p13-p12 resp. The expression profile in a panel of human tumor cell lines shows that GPC99 and GPC99a gene is involved in hyperproliferative conditions such as cancer. Up-regulation of GPC99 and GPC99a contributes to tumorigenesis and tumor development in a mammal. RAMP2 and RAMP3, as type I transmembrane proteins, interact with, and serve as co-receptors for, calcitonin receptor-like receptor (CRLR) or adrenomedullin (ADM). An anti-RAMP2 antibody is raised in rabbit using 18-aa peptide spanning a nonconserved 7-amino acid peptide close to the transmembrane region in the extracellular domain of RAMP2, which is critical for CRLR binding and adrenomedullin signaling. This antibody can induce apoptosis of human cancer cell lines through Annexin V and Caspase 3 stimulation. Thus various oligonucleotides of GPC99 and GPC99a are claimed as targets of siRNAs for cancer therapy, and related models for cancer treatments are also described.

L13 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:430723 Document No. 141:1219 Gene GPC15 involved in hyperproliferative conditions, and methods and compositions for treating and diagnosing cancer. O'Hagan, Ronan C.; Kannan, Karuppiiah (Genpath Pharmaceuticals, Incorporated, USA). PCT Int. Appl. WO 2004043408 A2 20040527, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US36799 20031113. PRIORITY: US 2002-2002/PV426489 20021113.

AB This invention provides methods and compns. for treating hyperproliferative conditions such as cancer using reagents relating to the GPC15 gene (also known as GP15). GPC15 was identified by the Mammalian Second Site Suppression ("MaSS") screening system. GPC15 gene is involved in hyperproliferative conditions such as cancer. Up-regulation of GPC15 contributes to tumorigenesis and tumor maintenance in a mammal. The GPC15 gene encodes ribosomal protein L29 (RPL29), which is a component of the large 60S ribosomal subunit. It also functions as a cell surface heparin/heparin sulfate binding protein. The GPC15 gene is expressed ubiquitously. The expression, however, is decreased in certain head & neck cancer, pancreatic cancer and ovarian cancer.

L13 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:252340 Document No. 140:264487 Medicaments containing disorazoles and derivatives thereof for the **treatment** of benign and malignant tumors. Irschik, Herbert; Jansen, Rolf; Sasse, Florenz; Baasner, Silke; Schmidt, Peter; Gunther, Eckhard (Zentaris GmbH, Germany). PCT Int. Appl. WO 2004024149 A1 20040325, 30 pp. DESIGNATED STATES: W: AT, AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2003-EP9329 20030822. PRIORITY: US 2002-2002/PV405594 20020824.

AB The invention discloses disorazole compds. which are used as medicaments, preferably in the **treatment** of tumors, especially in the case of drug resistance and in metastasizing carcinoma. Possible uses thereof are not restricted to tumor diseases.

L13 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:162782 Document No. 140:216175 FcγRIIB-specific antibodies and fragments for diagnosis and **treatment** of cancer, inflammation, autoimmune disease, allergy and immune disease. Koenig, Scott; Veri, Maria-Concetta (Macrogenics, Inc., USA). PCT Int. Appl. WO 2004016750 A2 20040226, 174 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US25399 20030814. PRIORITY: US 2002-2002/PV403266 20020814.

AB The present invention relates to antibodies or fragments thereof that specifically bind FcγRIIB, particularly human FcγRIIB, with greater affinity than said antibodies or fragments thereof bind FcγRIIA, particularly human FcγRIIA. The antibodies are humanized or chimeric derivs. of mouse monoclonal antibody 3H7 and 2B6. The invention provides methods of enhancing the therapeutic effect of therapeutic antibodies by administering the antibodies of the invention to enhance the effector function of the therapeutic antibodies. The invention also provides methods of enhancing efficacy of a vaccine composition by administering the antibodies of the invention.

L13 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2004:41276 Document No. 140:105251 3,4-Dihydroisoquinolin-1-one derivatives as inducers of apoptosis. Gangloff, Anthony R.; Litvak, Joane; Pararajasingham, Keith; Sperandio, David (Axys Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2004004727 A1 20040115, 107 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US21102 20030703. PRIORITY: US 2002-2002/PV394094 20020703.

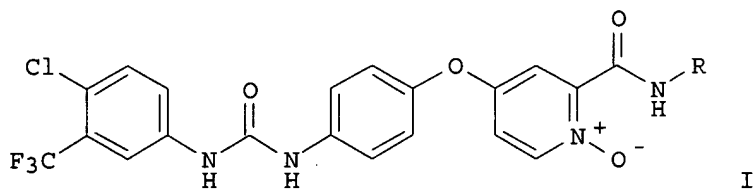
AB The invention discloses 3,4-dihydroisoquinolin-1-one derivs. that are activators of caspases and inducers of apoptosis, as well as pharmaceutical compns. comprising these compds., and methods for treating cancer using these compds. Preparation of selected compds. of the invention is included.

L13 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2003:656581 Document No. 139:197370 Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors. Dumas, Jacques; Scott, William J.; Riedl, Bernd (Bayer

Corporation, USA). PCT Int. Appl. WO 2003068229 A1 20030821, 67 pp.
 DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US4110 20030211. PRIORITY: US 2002-2002/PV354935 20020211.

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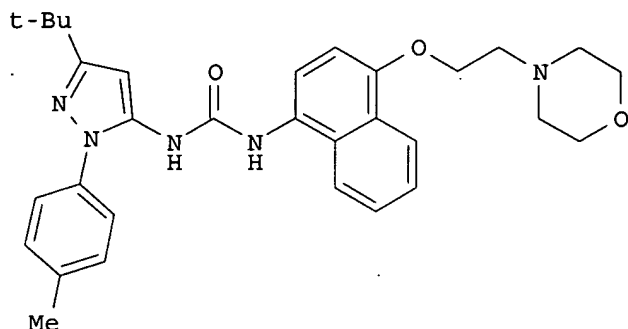


AB The title ureas containing a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH₂)_mO(CH₂)_l, (CH₂)_m(CH₂)_l, (CH₂)_mCO(CH₂)_l, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the **treatment** of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Preparation of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical composition comprising the title ureas was claimed.

L13 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2003:656575 Document No. 139:197476 Preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity. Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia (Bayer Corporation, USA). PCT Int. Appl. WO 2003068223 A1 20030821, 142 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US4102 20030211. PRIORITY: US 2002-2002/PV354948 20020211.

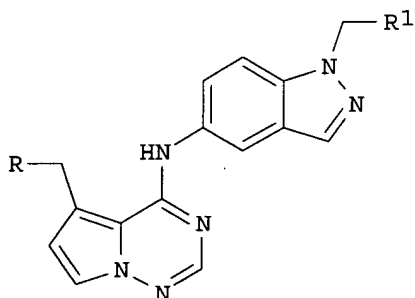
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AB 283 Of the title ureas useful for treating diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Synthesis of 6 ureas such as I was described. Thus, reacting 3-(tert-butyl)-1-(4-methylphenyl)pyrazole-5-ylamine with 4-(2-morpholin-4-ylethoxy)naphthylamine (preps. given) and CDI in CH₂Cl₂ afforded 80% I which showed IC₅₀ of < 1 μM in in vitro raf kinase and in in vitro Flk-1 ELISA assay.

L13 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2005 ACS on STM
 2003:396849 Document No. 138:401758 Preparation of 5-substituted N-(1H-indazol-5-yl)pyrrolo[2,1-f][1,2,4]triazin-4-amines as antiproliferative agents. Mastalerz, Harold; Zhang, Guifen; Tarrant, James G.; Vite, Gregory D. (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003042172 A2 20030522, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US36528 20021112. PRIORITY: US 2001-2001/PV333014 20011114.

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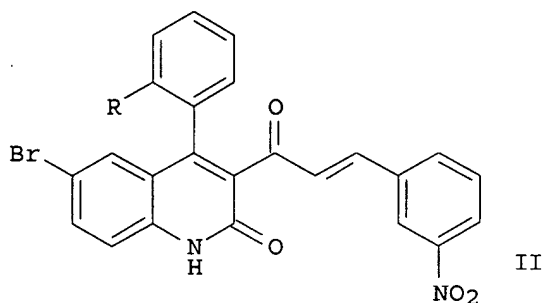
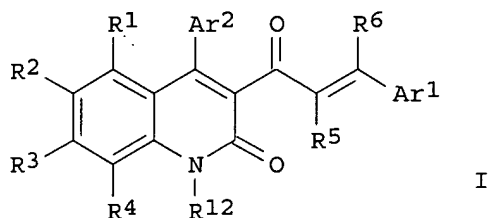


AB Title compds. I [wherein R = SR₂, SOR₂, SO₂R₂, OR₂, or NR₃R₄; R₁ = (un)substituted aryl or heterocyclyl; R₂ = H or (un)substituted alkyl, aryl, aralkyl, or heterocyclyl; R₃ and R₄ = independently H or (un)substituted alkyl, aryl, or heterocyclyl; or NR₃R₄ = (un)substituted heterocyclyl; and enantiomers, diastereomers, and pharmaceutically acceptable salts, prodrugs, and solvates thereof] were prepared as

inhibitors of tyrosine kinase activity of growth factor receptors, such as HER1, HER2 and HER4. For example, coupling of 5-bromomethyl-4-chloropyrrolo[2,1-f][1,2,4]triazine with benzenethiol in the presence of diisopropylethylamine in DCM, followed by addition of 1-(3-fluorobenzyl)-1H-indazol-5-ylamine in BuOH and 1,2-dichloroethane gave the phenylthio derivative I (R = PhS; R1 = 3-FC6H4) (II) in 58% yield. Oxidation with 3-chloroperbenzoic acid in chloroform provided the sulfinyl derivative I (R = PhSO; R1 = 3-FC6H4) (III) in 95% yield. I inhibited HER-1, HER-2, and HER-4 kinases with IC50 values between 0.001 μ M - 25 μ M. Thus, I are useful as antiproliferative agents and for the **treatment** of other diseases associated with signal transduction pathways operating through growth factor receptors (no data).

L13 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN
 2002:946113 Document No. 138:24647 Preparation of 4-aryl-3-(3-aryl-1-oxo-2-propenyl)-2(1H)-quinolinones and analogs as activators of caspases and inducers of apoptosis for **treatment** of cancer and other proliferative disorders. Cai, Sui Xiong; Zhang, Han-Zhong; Drewe, John; Kasibhatla, Shailaja (Cytovia, Inc., USA). PCT Int. Appl. WO 2002098425 A1 20021212, 66 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
 (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17486 20020604.
 PRIORITY: US 2001-2001/PV295007 20010604.

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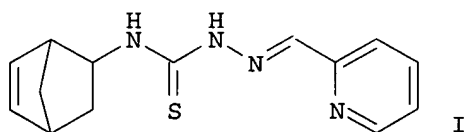
AB Title compds. I [wherein R1-R4 = independently H, halo, (hetero)aryl, (halo)alkyl, (hetero)cycloalkyl, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, hydroxyalkyl, NO2, NH2, CN, acylamino, OH, SH, acyloxy, azido, (halo)alkoxy, aryloxy, arylalkoxy, carboxy, carbonylamido, or alkylthio; R5, R6, and R12 = independently H or (un)substituted alkyl; Ar1 = (un)substituted (hetero)aryl, (partially) saturated carbocyclyl, or (partially) saturated heterocyclyl; Ar2 = (un)substituted (hetero)aryl; and

pharmaceutically acceptable salts or prodrugs thereof] were prepared as activators of caspases and inducers of apoptosis. For example, 2-amino-2'-fluoro-5-bromobenzophenone was treated with diketene in pyridine to give 3-acetyl-6-bromo-4-(2-fluorophenyl)-2(1H)-quinolinone (89%). Condensation with m-nitrobenzaldehyde in EtOH produced the (3-nitrophenylpropenoyl)quinolinone II (R = NO₂) in 42% yield. A related compound, II (R = H), activated caspase cascade activity with EC₅₀ values of 849 nM and 1800 nM against human breast cancer cell lines T-47D and ZR-75-1, resp. Thus, I may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs, such as cancer and other proliferative disorders.

L13 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2002:946109 Document No. 138:24718 Preparation of 4-substituted-1-(arylmethylidene)thiosemicarbazides and 4-substituted-1-(arylcarbonyl)thiosemicarbazides as activators of caspases and inducers of apoptosis. Cai, Sui Xiong; Nguyen, Bao Ngoc; Drewe, John; Reddy, P. Sanjeeva; Kasibhatla, Shailaja; Pervin, Azra (Cytovia, Inc., USA). PCT Int. Appl. WO 2002098420 A1 20021212, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17108 20020531. PRIORITY: US 2001-2001/PV294641 20010601.

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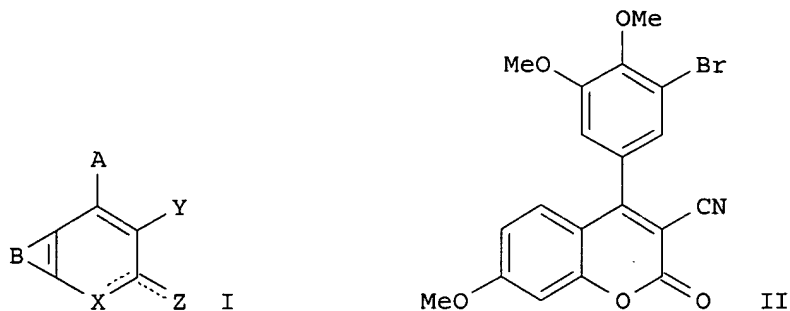


AB The title compds. A1NR1C(:Q)NR2N:CR3A2 and A1NR1C(:Q)NR2NR3C(:O)A2 [A1, A2 = (un)substituted aryl, heteroaryl, etc.; Q = S, O; R1-R3 = H, alkyl, cycloalkyl] which may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs, were prepared. Thus, reacting N1-bicyclo[2.2.1]hept-5-en-2-ylhydrazine-1-carbothioamide with 2-pyridinecarboxaldehyde in the presence of glacial AcOH in EtOH afforded 73% I which was identified as a potent caspase cascade activator and inducer of apoptosis in solid tumor cells (biol. data given).

L13 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2002:888548 Document No. 137:384750 Preparation of substituted coumarins and quinolinones as caspase activators for **treatment** of cancer. Cai, Sui Xiong; Zhang, Hong; Kemmitzer, William E.; Jiang, Songchun; Drewe, John A.; Storer, Richard (Cytovia, Inc., USA; Shire Biochem, Inc.). PCT Int. Appl. WO 2002092076 A1 20021121, 84 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US15401 20020516. PRIORITY: US 2001-2001/PV290978 20010516.

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AB Title compds. I [wherein X = O, S or NR₆; R₆ = H or (un)substituted alkyl or aryl; Y = CN, COR₇, CO₂R₇, or CONR₉R₁₀; R₇, R₉, and R₁₀ = independently H, (halo)alkyl, (fused) aryl, carbocyclyl, heterocyclyl, heteroaryl, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, (hetero)arylalkynyl, (hetero)cycloalkyl, hydroxyalkyl, or aminoalkyl; or NR₉R₁₀ = heterocyclyl; Z = O, S, halo, NR₈, or NCOR₈; R₈ = independently H, alkyl, or aryl; A = (un)substituted (hetero)aryl, (hetero)cyclyl, or (hetero)arylalkyl; B = (un)substituted (hetero)aryl or (hetero)cyclyl; or pharmaceutically acceptable salts or prodrugs thereof] were prepared as caspase activators and inducers of apoptosis. For example, condensation of 5-bromoveratraldehyde with Et cyanoacetate in EtOH in the presence of piperidine gave 3-(3-bromo-4,5-dimethoxyphenyl)-2-cyanoacrylic acid Et ester. **Treatment** of the acrylate with a solution of 3-methoxyphenol and NaH in toluene afforded the coumarin II (1.7%). The latter induced apoptosis in the human breast cancer cell lines T-47D and ZR-75-1 with EC₅₀ values of 257 nM and 97 nM, resp. Therefore, I, optionally administered with at least one known cancer chemotherapeutic agent, are useful for the **treatment** of cancer.

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2002:868695 Document No. 137:352786 Preparation of substituted N'-(arylcarbonyl)benzhydrazides and N'-(benzylidene)benzhydrazides and analogs as activators of caspases and inducers of apoptosis for use as antitumor agents. Cai, Sui Xiong; Kasibhatla, Shailaja; Drewe, John; Reddy, P. Sanjeeva; Zhang, Han-Zhong (Cytovia, Inc., USA). PCT Int. Appl. WO 2002089745 A2 20021114, 80 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US14722 20020510. PRIORITY: US 2001-PV289803 20010510.

AB The present invention is directed to substituted N'-(arylcarbonyl)benzhydrazides, N'-(arylcarbonyl)benzylidene hydrazides and analogs thereof, represented by Ar₁C(O)NR₂NR₁C(O)Ar₂ and Ar₁C(O)NR₂:CR₁Ar₂ (e.g. N'-(2-phenoxy-pyridine-3-carbonyl)-3-(trifluoromethyl)benzhydrazide (1)): wherein Ar₁ is optionally substituted pyridyl, pyrimidinyl or phenyl; Ar₂ is optionally substituted aryl or heteroaryl; and R₁ and R₂ are independently H, alkyl or cycloalkyl; with the proviso that said compound is other than 4-hydroxybenzoic acid (2-hydroxybenzylidene)hydrazide. The present invention also relates to the discovery that these compds. are activators of caspases and inducers of apoptosis and therefore may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. Although the methods of preparation are not claimed, 42 example preps. are included. Compound 1 and analogs were identified as caspase

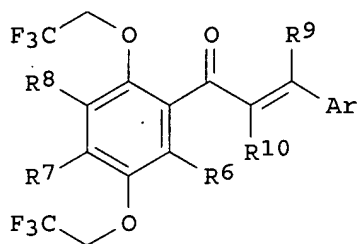
cascade activators and inducers of apoptosis in solid tumor cells and as antineoplastic compound that inhibits cell proliferation (GI50).

Treatment with 1 leads to cell cycle arrest and apoptosis in T-47D cells. Compound 1 and analogs were identified as antineoplastic compound that selectively inhibits the proliferation of breast cancer cells (GI50). Compound 1 was also found to inhibit the clonogenic survival of T47D and MX-1 solid tumor cell lines.

L13 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2002:716246 Document No. 137:247550 Preparation of multifluoro-substituted chalcones and analogs as activators of caspases and inducers of apoptosis. Cai, Sui Xiong; Reddy, P. Sanjeeva; Drewe, John A.; Nguyen, Bao Ngoc; Kasibhatla, Shailaja (Cytovia, Inc., USA). PCT Int. Appl. WO 2002072544 A2 20020919, 53 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US7569 20020314. PRIORITY: US 2001-2001/PV275473 20010314.

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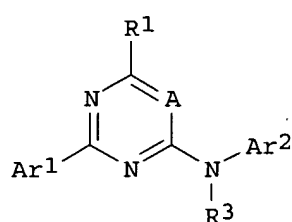


AB The title compds. [I; Ar = (un)substituted (hetero)aryl; R6-R10 = H, halo, haloalkyl, etc.] which are activators of caspases and inducers of apoptosis, and therefore may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs, were prepared Thus, reacting 2,5-bis(2,2,2-trifluoromethoxy)acetophenone with α,α,α -trifluoro-p-tolualdehyde afforded 13% I [Ar = 4-F₃CC₆H₄; R6-R10 = H] which was identified as antineoplastic compound that inhibits cell proliferation in a variety of cancer cell lines (data given).

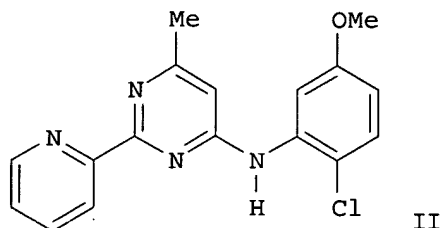
L13 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2002:465821 Document No. 137:47211 Substituted 2-aryl-4-arylamino-pyrimidines and analogs as activators of caspases and inducers of apoptosis, their preparation, and the use thereof as, e.g., anticancer agents. Cai, Sui Xiong; Drewe, John A.; Nguyen, Bao; Reddy, P. Sanjeeva; Pervin, Azra (Cytovia, Inc., USA). PCT Int. Appl. WO 2002047690 A1 20020620, 210 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US47498 20011212. PRIORITY: US 2000-PV254581 20001212.

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I



II

AB The invention is directed to substituted 2-aryl-4-(arylamino)pyrimidines I and analogs thereof [Ar1, Ar2 = (independently) optionally substituted aryl or heteroaryl; A = N or C-R2; R1, R2 = (independently) H, halo, haloalkyl, aryl, fused aryl, carbocyclic, heterocyclic, heteroaryl, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, amino, cyano, acylamido, OH, SH, acyloxy, N3, alkoxy, aryloxy, arylalkoxy, haloalkoxy, CO2H, carbonylamido, or alkylthio; and R3 = H, optionally substituted alkyl or cycloalkyl]. The invention also relates to the discovery that compds. I are activators of caspases and inducers of apoptosis. I may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. In particular, a method of treating disorders responsive to the induction of apoptosis, comprising administration of I, or a pharmaceutically acceptable salt or prodrug thereof, is claimed. Over 200 specific examples of I are described. For instance, condensation of 4-chloro-6-methyl-2-(2-pyridinyl)pyrimidine with 2-chloro-5-methoxyaniline gave title compound II in 44% yield. This compound induced apoptosis and activated caspase cascade in human breast cancer cell lines T-47D and ZR-75-1. Another compound I also showed marked selectivity for human breast cancer cells over other, non-breast cancer cell lines.

L13 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2002:449519 Document No. 137:28278 Methods of **treatment** of angiogenesis-related disease involving human MDA-7 protein. Chada, Sunil; Grimm, Elizabeth; Mhashilkar, Abner; Schrock, Bob; Rajagopal, Ramesh (University of Texas, USA). PCT Int. Appl. WO 2002045737 A2 20020613, 159 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US47215 20011207. PRIORITY: US 2000-2000/PV254226 20001207.

AB The invention relates to gene therapy methods for the **treatment** of human disease. More specifically, the invention is directed to methods for treating a subject with an angiogenesis-related disease. In one embodiment, an adenoviral expression construct comprising a nucleic acid encoding a human MDA-7 protein under the control of a promoter operable in eukaryotic cells, is administered to said patient with a angiogenesis-related disease. The present invention thus provides for **treatment** of angiogenesis-related disease by through expression of mda-7 and inhibition angiogenesis. Such diseases include cancer.

L13 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2001:798040 Document No. 135:339222 Inhibition of abnormal cell proliferation with camptothecin or a derivative, analog, metabolite, or prodrug thereof, and combinations including camptothecin. Rubinfeld, Joseph (Supergen, Inc., USA). PCT Int. Appl. WO 2001080843 A2 20011101,

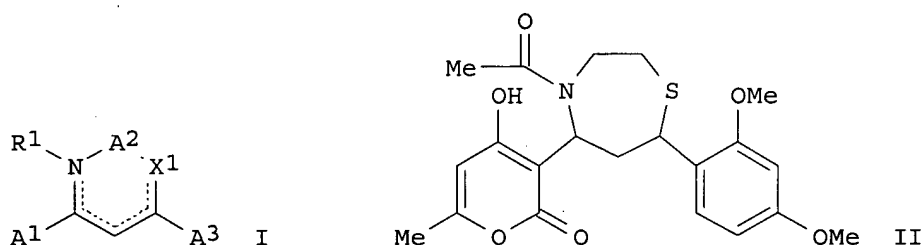
38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US12848 20010419. PRIORITY: US 2000-553710 20000420.

AB A method for treating diseases associated with abnormal cell proliferation comprises delivering to a patient in need of **treatment** a compound selected from 20(S)-camptothecin, an analog of 20(S)-camptothecin, a derivative of 20(S)-camptothecin, a prodrug of 20(S)-camptothecin, and pharmaceutically active metabolite of 20(S)-camptothecin, in combination with an effective amount of one or more agents selected from the group consisting of alkylating agent, antibiotic agent, antimetabolic agent, hormonal agent, plant-derived agent, anti-angiogenesis agent and biol. agent. The method can be used to treat benign tumors, malignant or metastatic tumors, leukemia and diseases associated with abnormal angiogenesis.

L13 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2001:780869 Document No. 135:331449 Preparation of substituted 1,4-thiazepines and analogs as activators of caspases and inducers of apoptosis for **treatment** of cancer and other proliferative diseases. Cai, Sui Xiong; Drewe, John A.; Shelton, Emma Jane; Litvak, Joane; Sperandio, David; Spencer, Jeffrey R. (Cytovia, Inc., USA). PCT Int. Appl. WO 2001079187 A2 20011025, 162 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US12581 20010418. PRIORITY: US 2000-PV197599 20000418.

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AB Title compds. I [wherein R1 = null, H, alkyl, or COR6; X1 = NR2, S, SO, SO2, or O; R6 = null, H, or (halo)alkyl; A1 = (un)substituted monocyclic or fused polycyclic (hetero)aryl or (hetero)cycloalkyl ring; or A1 and R1 together form an (un)substituted fused polycyclic heteroaryl or heterocycloalkyl ring; the ring containing A2 = (un)substituted monocyclic or fused bicyclic heteroarylene or heterocycloalkylene ring; A3 = (un)substituted monocyclic or fused polycyclic (hetero)aryl or (hetero)cycloalkyl ring; and N-oxides, prodrugs, protected derivs., stereoisomers, and pharmaceutically acceptable salts thereof] were prepared as caspase activators and apoptosis inducers. For example, coupling of 3-acetyl-4-hydroxy-6-methylpyran-2-one with 2,4-dimethoxybenzaldehyde, followed by cyclization with 2-aminoethanethiol (61%) and acetylation, gave the [1,4]thiazepine II. Five invention compds. were tested and

demonstrated caspase potency in human breast cancer cell lines T-47D and ZR-75-1 with EC50 values ranging from 345 nM to 6930 nM and 163 nM to 4207 nM, resp. Thus, I and their compns. with known cancer chemotherapeutic agents are useful for the **treatment** of drug resistant cancer in animals.

L13 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

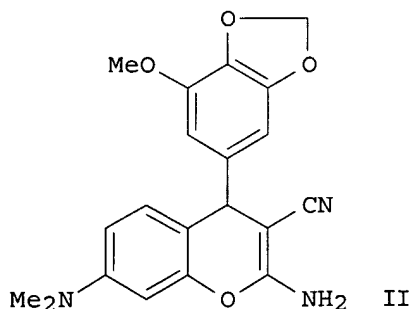
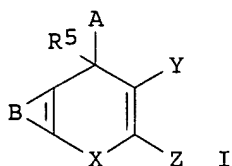
2001:380440 Document No. 135:18554 Targeted delivery of therapeutic and diagnostic moieties. Press, Michael; Park, Jinha (University of Southern California, USA). PCT Int. Appl. WO 2001036005 A2 20010525, 66 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US31424 20001115. PRIORITY: US 1999-PV165563 19991115.

AB Compns. and methods for improving cellular internalization of one or more compds. are disclosed. The invention provides a drug conjugate composition that can be delivered to a target cell, which comprises a carrier compound that has a binding specificity for a receptor mol. and is conjugated to a therapeutic or diagnostic moiety. When this composition is administered to a subject, the carrier compound binds to the receptor and is internalized by the target cell. Furthermore, monoclonal antibodies are disclosed that are internalized into target cells. The monoclonal antibodies of the invention are specific for target cells, particularly for cells expressing the surface antigen p185HER-2. The antibodies of the invention may be conjugated with a mol. for delivery into a target cell. Such mols. may be used for therapeutic **treatment**, including gene therapy, and for imaging. The invention also provides DNA sequences of the variable regions of particular monoclonal antibodies.

L13 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2001:359984 Document No. 134:353254 Substituted 4H-chromene and analogs as activators of caspases and inducers of apoptosis and the use thereof. Drewe, John A.; Cai, Sui Xiong; Wang, Yan (Cytovia, Inc., USA). PCT Int. Appl. WO 2001034591 A2 20010517, 148 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US30374 20001103. PRIORITY: US 1999-PV163584 19991105; US 2000-PV185211 20000224.

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AB Title compds. (I) [wherein X = O or S; Y = CN, COR7, CO2R7, or CONRxRy; R7, Rx, and Ry = independently H, (halo)alkyl, (hetero)aryl, fused aryl, carbocyclic, heterocyclic, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, (hetero)arylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, or aminoalkyl; or Rx and Ry taken together with the N to which they are attached form a heterocycle; Z = NR8R9, NHCOR8, N(COR8)2, N(COR8)(COR9), N:CHOR8, or N:CHR8; R8 and R9 = independently H, alkyl, or aryl; or R8 and R9 taken together with the group to which they are attached form a heterocycle; R5 = H or alkyl; A = (un)substituted (hetero)aryl, carbocyclic, heterocyclic, or arylalkyl; B = (un)substituted (hetero)aromatic ring] were prepared as activators of caspases and inducers of apoptosis. For example, piperidine was added to a mixture of 3-dimethylaminophenol, 5-methoxypiperonal, and malonitrile in EtOH to give II (74%). In assays against the human breast cancer cell lines T-47D and ZR-75-1, II showed potent caspase activity (determined as the ratios of net relative fluorescence units for test compds. compared to control samples of 5.5 and 6.3, resp.) and potency (EC50 = 87 nM and 38 nM, resp.). II also inhibited cell proliferation with GI50 values of 3 nM and 500 nM against T-47D and ZR-75-1, resp. Thus, I may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

L13 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2001:63858 Document No. 134:125935 Methods for **treatment** of hyperproliferative diseases using human MDA-7. Mhashilkar, Abner; Schrock, Bob; Chada, Sunil (Introgen Therapeutics, Inc., USA). PCT Int. Appl. WO 2001005437 A2 20010125, 161 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US19392 20000713. PRIORITY: US 1999-PV144354 19990715; US 2000-PV200768 20000428.

AB The present invention relates to gene therapy methods for the **treatment** of human disease. More specifically, the invention is directed, in one embodiment, to methods for treating a subject with a hyperproliferative disease. In another embodiment, an adenoviral expression construct comprising a nucleic acid encoding a human MDA-7 protein under the control of a promoter operable in eukaryotic cells is administered to the patient with a hyperproliferative disease. The present invention thus provides a gene therapy for treating hyperproliferative disease by elevating the expression of MDA-7 resulting in inhibition of cell growth and induction of apoptosis in hyperproliferative cells.

L13 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2005 ACS on STN

2001:851786 Document No. 136:4707 Immunostimulatory nucleic acids for inducing a Th2 immune response. McCluskie, Michael J.; Davis, Heather L. (Can.). U.S. Pat. Appl. Publ. US 2001044416 A1 20011122, 50 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-768012 20010122. PRIORITY: US 2000-2000/PV177461 20000120.

AB The invention relates to methods and products for inducing an immune response using immunostimulatory nucleic acids. In particular the immunostimulatory nucleic acids preferentially induce a Th2 immune response. The invention is useful for treating and preventing disorders associated with a Th1 immune response or for creating a Th2 environment for treating disorders that are sensitive to Th2 immune responses. These disorders include Th1-mediated disease, autoimmune disease, infection, and cancer.

=> s psoriasis

L14 83799 PSORIASIS

=> s l14 and treatment

L15 29955 L14 AND TREATMENT

=> s l15 and antibod?

L16 2565 L15 AND ANTIBOD?

=> s l16 and HER2

L17 5 L16 AND HER2

=> dup remove l17

PROCESSING COMPLETED FOR L17

L18 5 DUP REMOVE L17 (0 DUPLICATES REMOVED)

=> d l18 1-5 cbib abs

L18 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

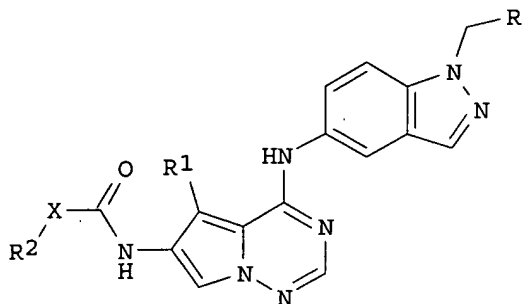
2004:965067 Document No. 141:406039 Combinations for the **treatment** of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A. (Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.). PCT Int. Appl. WO 2004096224 A2 20041111, 101 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-EP4363 20040424. PRIORITY: EP 2003-9587 20030429; EP 2004-508 20040113; EP 2004-1171 20040121.

AB The present invention relates to a pharmaceutical combination for the **treatment** of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the **treatment** of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-**treatment** with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepn's. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

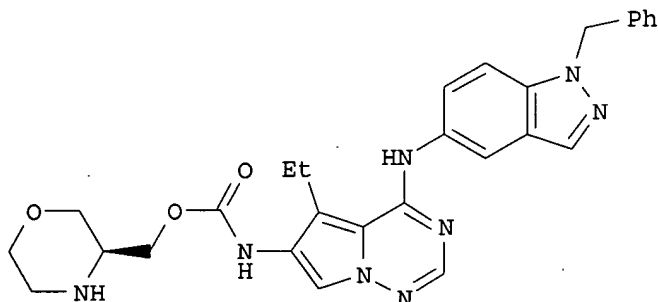
L18 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

2004:531311 Document No. 141:89122 Preparation of C-6 modified indazolyl pyrrolotriazines as antiproliferative agents. Vite, Gregory D.; Gavai, Ashvinikumar V.; Fink, Brian E.; Mastalerz, Harold; Kadow, John F. (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2004054514 A2 20040701, 81 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US39542 20031212. PRIORITY: US 2002-2002/PV433190 20021213.

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I



II

AB The title compds. [I; R = (un)substituted aryl, heterocyclyl; R1 = (un)substituted alkyl; R2 = H, (un)substituted alkyl, cycloalkyl, aryl, etc.; X = a bond, O, S, (un)substituted NH, etc.] and their pharmaceutically acceptable salts which inhibit tyrosine kinase activity of growth factor receptors such as HER1, **HER2** and HER4 thereby making them useful as antiproliferative agents, were prepared E.g., a multi-step synthesis of (3S)-II.HCl, starting from 5-nitroindazole, was given. Preferred compds. I exhibit IC50 of < 5 μ M in one or more of HER1, **HER2** and HER4 assays. The compds. I are also useful for the **treatment** of other diseases associated with signal transduction pathways operating through growth factor receptors. The pharmaceutical composition comprising the compound I is claimed.

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

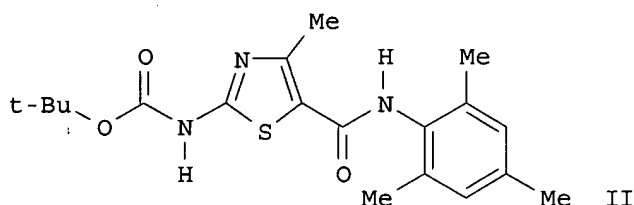
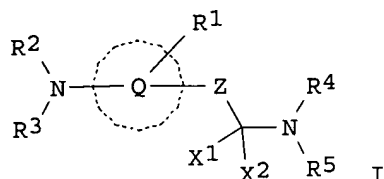
2004:467984 Document No. 141:22217 Therapy of non-malignant diseases or disorders with anti-ErbB2 **antibodies**. Sliwkowski, Mark X.; Brunetta, Paul G. (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized **antibodies** to **HER2**. In one example, an anti-**HER2** antibody is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes **treatment** of non-malignant indications, such as **psoriasis**, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with anti-ErbB2 **antibodies** (e.g. rhuMAb 2C4).

L18 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

2004:220082 Document No. 140:253556 Preparation of 5-thiazolecarboxamides as protein tyrosine kinase inhibitors. Das, Jagabandhu; Padmanabha, Ramesh; Chen, Ping; Norris, Derek J.; Doweiko, Arthur M. P.; Barrish, Joel C.; Wityak, John; Lombardo, Louis J.; Lee, Francis Y. F. (USA). U.S. Pat. Appl. Publ. US 2004054186 A1 20040318, 184 pp., Cont.-in-part of U.S. 6,596,746. (English). CODEN: USXXCO. APPLICATION: US 2003-395503 20030324. PRIORITY: US 1999-PV129510 19990415; US 2000-2000/548929 20000413.

GI



AB The title compds. [I; Q = (un)substituted 5-6 membered heteroaryl, aryl; Z = a single bond, R15C:CH, (CH2)m (m = 1-2); X1, X2 = H; X1 and X2 together = O, S; R1 = H, alkyl, alkenyl, etc.; R2, R3 = H, alkyl, alkenyl, etc.; R4, R5 = H, alkyl, alkenyl, etc.], useful in the **treatment** of protein tyrosine kinase-associated disorders such as immunol. and oncol. disorders (no data), were prepared E.g., a multi-step synthesis of thiazole II was given. Compds. I are effective at 0.1-100 mg/kg/day. The pharmaceutical composition comprising the title compds. is claimed.

L18 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STM

2000:210344 Document No. 132:247117 Cell proliferative disease diagnosis method by cytosine methylation analysis in cytokine receptor gene. Homma, Yoshimi; Oyama, Noritaka; Sato, Koichiro (Kyowa Hakko Kogyo Co., Ltd., Japan). PCT Int. Appl. WO 2000017339 A1 20000330, 31 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CN, CZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1999-JP5069 19990917. PRIORITY: JP 1998-265089 19980918.

AB Methods for the diagnosis of a cell proliferative disease characterized by analyzing the extent of the methylation of cytosine residues in a region associated with the expression of a cytokine receptor gene are disclosed. **Psoriasis** was diagnosed by analyzing the extent of CpG island cytosine residues in the promoter region of epidermal growth factor receptor (EGF-R) gene via sodium sulfite **treatment** and PCR amplification. Chronic rheumatoid arthritis was similarly diagnosed by analyzing the extent of CpG island cytosine residues in the promoter region of epidermal growth factor receptor 2 (erbB2/**HER2**/neu) gene.

=> s 116 and anti-HER2

L19 1 L16 AND ANTI-HER2

=> d l19 cbib abs

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

2004:467984 Document No. 141:22217 Therapy of non-malignant diseases or disorders with anti-ErbB2 **antibodies**. Sliwkowski, Mark X.; Brunetta, Paul G. (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized **antibodies** to HER2. In one example, an **anti-HER2 antibody** is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes **treatment** of non-malignant indications, such as **psoriasis**, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with anti-ErbB2 **antibodies** (e.g. rhuMab 2C4).

=> s l16 and anti-ErbB2

L20 1 L16 AND ANTI-ERBB2

=> d l20 cbib abs

L20 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

2004:467984 Document No. 141:22217 Therapy of non-malignant diseases or disorders with anti-ErbB2 **antibodies**. Sliwkowski, Mark X.; Brunetta, Paul G. (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized **antibodies** to HER2. In one example, an anti-HER2 **antibody** is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes **treatment** of non-malignant indications, such as **psoriasis**, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with **anti-ErbB2 antibodies** (e.g. rhuMab 2C4).

=> d his

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 14:03:59 ON 19 OCT 2005

L1 247 S ERBB2 ANTIBOD?
L2 96 S L1 AND TREATMENT
L3 1 S L2 AND NON-MALIGNANT

L4 2735552 S ANTIBOD?
 L5 1117 S L4 AND ANTI-HER2
 L6 0 S L5 AND ANTI-P185NEU
 L7 8 S L5 AND ANTI-P185
 L8 4 DUP REMOVE L7 (4 DUPLICATES REMOVED)
 L9 4927 S HERCEPTIN
 L10 2284 S L9 AND TREATMENT
 L11 1 S L10 AND NON-MALIGNANT
 L12 30 S L10 AND PSORIASIS
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 L15 29955 S L14 AND TREATMENT
 L16 2565 S L15 AND ANTIBOD?
 L17 5 S L16 AND HER2
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 L20 1 S L16 AND ANTI-ERBB2

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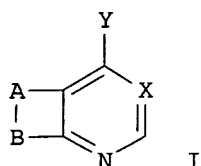
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L23 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 2004:467984 Document No. 141:22217 Therapy of non-malignant diseases or disorders with anti-ErbB2 **antibodies**. Sliwkowski, Mark X.; Brunetta, Paul G. (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized **antibodies** to HER2. In one example, an anti-HER2 **antibody** is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes **treatment** of non-malignant indications, such as **psoriasis**, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with anti-ErbB2 **antibodies** (e.g. rhuMAB 2C4).

L23 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 2004:200102 Document No. 140:235750 Preparation of quinazolines as epidermal growth factor receptor (**erbB**) inhibitors for the **treatment** of proliferative diseases. Kath, John Charles; Tom, Norma Jacqueline; Cox, Eric David; Bhattacharya, Samit Kumar (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1396489 A1 20040310, 26 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY. (English). CODEN: EPXXDW. APPLICATION: EP 2003-24331 19991224. PRIORITY: US 1999-PV117341 19990127; EP 1999-310574 19991224.

GI



AB Title compds. I [X = N, CH; A-B = R4-substituted fused pyridyl, pyrimidyl, furanyl, etc.; Y = NR1R3; R1, R2 = H, alkyl; R3 = -(CR1R2)m-R8 or R1 and R3 are taken together with N; R4 = -(CR1R2)p-aryl, -(CR1R2)p-heterocyclic, -(CR1R2)q-NR1R9, etc.; R8 = -(CR1R2)p-aryl, -(CR1R2)p-heterocyclic; R9 = fused or bridged bicyclic ring, spirocyclic ring with provisos; m= 0, 1; p, q = 0-5] and their pharmaceutically acceptable salts were prepared For example, coupling of compound I [X = N; A-B = -CR4=CH-CH=CH-; Y = OPh; R4 = 4-((6-hydroxymethyl-3-aza-bicyclo[3.1.0]hex-3-yl)methyl)phenyl], e.g., prepared from 6-iodo-4-quinazolinone in 4-steps, with 1-cyclopropylmethyl-1H-indol-5-ylamine, afforded compound I [X = N; A-B = -CR4=CH-CH=CH-; Y = 1-cyclopropylmethyl-1H-indol-5-ylamino; R4 = 4-((6-hydroxymethyl-3-aza-bicyclo[3.1.0]hex-3-yl)methyl)phenyl] in 67% yield. In c-erbB2 kinase inhibition assays, compds. I showed potent (sic.) inhibition of the erbB2 tyrosine kinase activity (no data provided). Compds. I are claimed useful for the **treatment** of cancer and benign proliferative diseases, e.g., **psoriasis**.

L23 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

2000:841957 Document No. 133:366470 Methods and compositions for non-viral gene therapy for **treatment** of hyperproliferative diseases. Ramesh, Rajagopal; Roth, Jack A.; Saeki, Tomoyuki; Wilson, Deborah (Introgen Therapeutics, Inc., USA; Board of Regents, the University of Texas System). PCT Int. Appl. WO 2000071096 A2 20001130, 148 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US14350 20000524. PRIORITY: US 1999-PV135818 19990524.

AB The present invention relates to non-viral gene therapy methods and compns. for **treatment** of hyperproliferative disease in humans. More specifically, the invention is directed, in one embodiment, to lipid formulations which form stable liposome structures, capable of efficient in vivo nucleic acid transfer. In other embodiments, methods and compns. are directed to liposome transfer of anti-proliferative nucleic acids, wherein the transfer of the nucleic acids is cell specific via cell specific targeting moieties. The present invention thus provides non-viral, liposome compns. and methods of gene transfer particularly useful for targeting and treating hyperproliferative disease.

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L24 555 (BRUNETTA P?/AU OR SLIWKOWSKI M?/AU)

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L26 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2004:467984 Document No. 141:22217 Therapy of non-malignant diseases or disorders with **anti-ErbB2** antibodies.

Sliwkowski, Mark X.; Brunetta, Paul G. (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized antibodies to HER2. In one example, an anti-HER2 antibody is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes treatment of non-malignant indications, such as psoriasis, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with **anti-ErbB2** antibodies (e.g. rhuMab 2C4).

L26 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2004:59563 Document No. 140:122766 Treatment of cancer with **anti-ErbB2** antibodies. Kelsey, Stephen M.; **Sliwkowski, Mark X.** (Genentech, Inc., USA). U.S. Pat. Appl. Publ. US 2004013667 A1 20040122, 56 pp., Cont.-in-part of U.S. Ser. No. 268,501. (English). CODEN: USXXCO. APPLICATION: US 2003-608626 20030627. PRIORITY: US 1999-PV141316 19990625; US 2000-2000/602812 20000623; US 2002-2002/268501 20021010.

AB The present application describes methods for treating cancer with **anti-ErbB2** antibodies, such as **anti-ErbB2** antibodies that block ligand activation of an ErbB receptor. Recombinant humanized monoclonal antibody 2C4 was effective in inhibiting breast cancer tumor growth in mice with MCF7 xenografts.

L26 ANSWER 3 OF 9

MEDLINE on STN

DUPLICATE 1

2004:165913. PubMed ID: 15059917. Blockade of epidermal growth factor- or heregulin-dependent ErbB2 activation with the **anti-ErbB2** monoclonal antibody 2C4 has divergent downstream signaling and growth effects. Jackson James G; St Clair Patricia; **Sliwkowski Mark X**; Brattain Michael G. (Department of Surgery, University of Texas Health Science Center, San Antonio, Texas, USA.) Cancer research, (2004 Apr 1) 64 (7) 2601-9. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB Due to heterodimerization and a variety of stimulating ligands, the ErbB receptor system is both diverse and flexible, which proves particularly advantageous to the aberrant signaling of cancer cells. However, specific mechanisms of how a particular receptor contributes to generating the flexibility that leads to aberrant growth regulation have not been well described. We compared the utilization of ErbB2 in response to epidermal growth factor (EGF) and heregulin stimulation in colon carcinoma cells. **Anti-ErbB2** monoclonal antibody 2C4 blocked heregulin-stimulated phosphorylation of ErbB2 and ErbB3; activation of mitogen-activated protein kinase (MAPK), phosphatidylinositol 3'-kinase (PI3K), and Akt; proliferation; and anchorage-independent growth. 2C4 blocked EGF-mediated phosphorylation of ErbB2 and inhibited PI3K/Akt and anchorage-independent growth but did not affect ErbB1 or MAPK. Immunoprecipitations showed that ErbB3 and Grb2-associated binder (Gab) 1 were phosphorylated and associated with PI3K activity after heregulin treatment and that Gab1 and Gab2, but not ErbB3, were phosphorylated and associated with PI3K activity after EGF treatment. These data show that monoclonal antibody 2C4 inhibited all aspects of heregulin signaling as

well as anchorage-independent and monolayer growth. Furthermore, we identify ErbB2 as a critical component of EGF signaling to the Gab1/Gab2-PI3K-Akt pathway and anchorage-independent growth, but EGF stimulation of MAPK and monolayer growth can occur efficiently without the contribution of ErbB2.

L26 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 2
 2004193989. PubMed ID: 15093539. Insights into ErbB signaling from the structure of the ErbB2-pertuzumab complex. Franklin Matthew C; Carey Kendall D; Vajdos Felix F; Leahy Daniel J; de Vos Abraham M; Sliwkowski Mark X. (Department of Protein Engineering, Genentech, Inc., 1 DNA Way, South San Francisco, CA 94114 USA.) Cancer cell, (2004 Apr) 5 (4) 317-28. Journal code: 101130617. ISSN: 1535-6108. Pub. country: United States. Language: English.

AB We have determined the 3.2 Å X-ray crystal structure of the extracellular domain of the human epidermal growth factor receptor 2 (ErbB2 or HER2) in a complex with the antigen binding fragment of pertuzumab, an anti-ErbB2 monoclonal antibody also known as 2C4 or Omnitarg. Pertuzumab binds to ErbB2 near the center of domain II, sterically blocking a binding pocket necessary for receptor dimerization and signaling. The ErbB2-pertuzumab structure, combined with earlier mutagenesis data, defines the pertuzumab residues essential for ErbB2 interaction. To analyze the ErbB2 side of the interface, we have mutated a number of residues contacting pertuzumab and examined the effects of these mutations on pertuzumab binding and ErbB2-ErbB3 heterodimerization. We have also shown that conserved residues previously shown to be necessary for EGF receptor homodimerization may be dispensable for ErbB2-ErbB3 heterodimerization.

L26 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 2003:355612 Document No. 138:362649 Treatment of cancer with anti-ErbB2 antibodies. Sliwkowski, Mark X. (Genentech, Inc., USA). U.S. Pat. Appl. Publ. US 2003086924 A1 20030508, 56 pp., Cont.-in-part of U.S. Ser. No. 602,812. (English). CODEN: USXXCO. APPLICATION: US 2002-268501 20021010. PRIORITY: US 1999-PV141316 19990625; US 2000-2000/602812 20000623.

AB The present application describes methods for treating cancer with anti-ErbB2 antibodies, such as anti-ErbB2 antibodies that block ligand activation of an ErbB receptor. Recombinant humanized monoclonal antibody 2C4 was effective in inhibiting breast cancer tumor growth in MCF7 xenografts.

L26 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 2002:409473 Document No.: PREV200200409473. Blockade of ErbB2 activation with the anti-ErbB2 monoclonal antibody 2C4 has divergent downstream signaling and growth effects following stimulation by epidermal growth factor or heregulin. Jackson, James G. [Reprint author]; St Clair, Patricia; Sliwkowski, Mark X.; Brattain, Michael G.. University of Texas Health Science Center at San Antonio, San Antonio, TX, USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 830-831. print. Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002. ISSN: 0197-016X. Language: English.

L26 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 2001:12297 Document No. 134:99574 Treating prostate cancer with anti-ErbB2 antibodies. Agus, David B.; Scher, Howard I.; Sliwkowski, Mark X. (Genentech, Inc., USA; Sloan-Kettering Institute for Cancer Research). PCT Int. Appl. WO 2001000238 A1 20010104, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US17423 20000623. PRIORITY: US 1999-PV141315 19990625.

AB The present application discloses treatment of prostate cancer with **anti-ErbB2** antibodies. These antibodies are combined with chemotherapeutic agent, cytokine, antiangiogenic agent, EGFR-targeted drug, antiandrogen, anthracycline antibiotic, etc. for treating androgen-(in)dependent prostate cancer.

L26 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 3

97472144. PubMed ID: 9333014. Gamma-heregulin: a novel heregulin isoform that is an autocrine growth factor for the human breast cancer cell line, MDA-MB-175. Schaefer G; Fitzpatrick V D; **Sliwkowski M X**. (Genentech, Inc., South San Francisco, California 94080, USA.) Oncogene, (1997 Sep 18) 15 (12) 1385-94. Journal code: 8711562. ISSN: 0950-9232. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A novel neuregulin isoform, termed gamma-HRG, was cloned and characterized from the human breast cancer cell line, MDA-MB-175. As observed with other neuregulins, gamma-HRG, is a product of alternative mRNA splicing of the neuregulin gene. Gamma-HRG contains the EGF-like and immunoglobulin-like domains that are commonly found in other family members, but lacks a transmembrane and cytoplasmic region. The new isoform possesses a unique N-terminal region that includes a hydrophobic domain that may function as a secretion signal. A purified recombinant version of gamma-HRG competes for binding to soluble ErbB3- and ErbB4-IgG fusion proteins with affinities similar to those observed for rHRGbeta1(177-244). Gamma-HRG has a wide distribution in mesenchymal or neuronal tissues but in contrast to other neuregulins, it is not present in breast, lung, liver and small intestine. Expression of gamma-HRG with its cognate receptors, ErbB3 and ErbB2 suggested that the growth of the MDA-MB-175 cell line might be a result of the autocrine stimulation of a growth factor signaling pathway. Treatment of MDA-MB-175 cells with an **anti-ErbB2** monoclonal antibody that interferes with the ligand-dependent formation of ErbB2-ErbB3 heterodimer complexes shows a strong growth inhibitory effect on this cell line. Moreover, incubation with a receptor-IgG fusion protein that neutralizes secreted gamma-HRG, also inhibits cell growth. These data suggest that the secretion of gamma-HRG by MDA-MB-175 cells leads to the formation of a constitutively active receptor complex and stimulates the growth of these cells in an autocrine manner.

L26 ANSWER 9 OF 9 MEDLINE on STN DUPLICATE 4

96189328. PubMed ID: 8640840. Growth regulation of human breast and ovarian tumor cells by heregulin: Evidence for the requirement of ErbB2 as a critical component in mediating heregulin responsiveness. Lewis G D; Lofgren J A; McMurtrey A E; Nuijens A; Fendly B M; Bauer K D; **Sliwkowski M X**. (Genentech, Inc., South San Francisco, California 94080, USA.) Cancer research, (1996 Mar 15) 56 (6) 1457-65. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB Alterations in the expression of the epidermal growth factor (EGF) receptor ErbB family are frequently encountered in a number of human cancers. Two of these receptors, ErbB3 and ErbB4, are known to bind a family of related proteins termed heregulins (HRGs) or neu differentiation factors. In biologically relevant systems, interaction of HRG with ErbB3 or ErbB4 results in the transactivation of ErbB2. In this report, we show that ErbB2 is a critical component in mediating HRG responsiveness in a panel of human breast and ovarian tumor cell lines. Because HRGs have been reported to elicit diverse biological effects on cultured cells, including growth stimulation, growth inhibition, and induction of differentiation, we systematically examined the effect of rHRG beta 1 on tumor cell proliferation. HRG binding studies were performed with a panel of breast and ovarian tumor cell lines expressing a range of levels of ErbB2. The biological responses to HRG were also compared to EGF and to

the growth-inhibitory anti-ErbB2 antibody, 4D5. In most cases, HRG stimulation of DNA synthesis correlated with positive effects on cell cycle progression and cell number and with enhancement of colony formation in soft agar. On each cell line tested, the HRG effects were distinguishable from EGF and 4D5. Our findings indicate that HRG induces cell proliferation in a number of tumor cell lines. In addition, we show that methods for measuring cell proliferation, as well as experimental conditions, are critical for determining HRGs effect on tumor cell growth in vitro.

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L28 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
2005:588702 Document No. 143:114050 Antagonists of CD20 in therapy of autoimmune diseases. **Brunetta, Paul G.** (Genentech, Inc., USA). PCT Int. Appl. WO 2005060999 A2 20050707, 51 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US40949 20041207. PRIORITY: US 2003-2003/PV531363 20031219.

AB The author discloses a method of treating autoimmune disease comprising; (a) detection of CD20 in a sample; (2) administration of a CD20 antagonist in an amount effective to treat the autoimmune disease.

L28 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
2004:467984 Document No. 141:22217 Therapy of non-malignant diseases or disorders with anti-ErbB2 antibodies. **Sliwkowski, Mark X.; Brunetta, Paul G.** (Genentech, Inc., USA). PCT Int. Appl. WO 2004048525 A2 20040610, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US37367 20031121. PRIORITY: US 2002-2002/PV428027 20021121.

AB The authors disclose the preparation and biol. activity of murine and humanized antibodies to HER2. In one example, an anti-HER2 antibody is shown to inhibit heregulin-induced activation of Akt kinase and erbB2 association with erbB3. The present application describes treatment of non-malignant indications, such as psoriasis, endometriosis, scleroderma, vascular diseases or disorders, respiratory disease, colon polyps or fibroadenoma, with anti-ErbB2 antibodies (e.g. rhuMAb 2C4).

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FULL ESTIMATED COST	216.33	216.54
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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